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Ervayunine: A New Indole Alkaloid from *Ervatamia yunnanensis*

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Received: December 16, 1987

Abstract: Nine indole alkaloids have been isolated from the roots of *Ervatamia yunnanensis* and identified as: heyneanine (1), ibogamine (2), coronaridine (3), voacangine (4), voacangine hydroxyindolenine (5), ibogaine (6), (+)-minovincine (7), voachalotin (8), and a new compound named ervayunine (9). The structure of ervayunine has been determined from physical and spectral data.

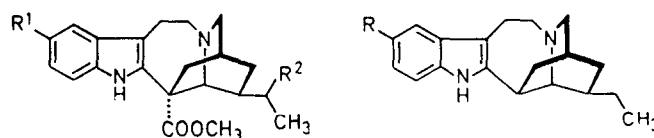
Introduction

There are 120 species belonging to the genus *Ervatamia*, among which 15 species and 5 varieties are known to be present in China (1).

Ervatamia yunnanensis Tsiang (Apocynaceae), called Yunnan gou ya hua in China, is a shrub or arbor distributed in the Yunnan and Guangxi provinces (2). The plant has been used in Chinese folk medicine for the treatment of hypertension. The chemistry of this plant has not been studied previously. Now we report the results of investigations on the chemical constituents of *Ervatamia yunnanensis*.

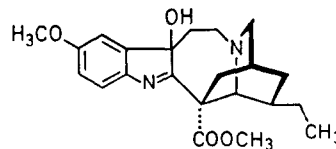
Results and Discussion

Nine indole alkaloids have been isolated from the roots of *Ervatamia yunnanensis*. Eight of them are known and identified as: heyneanine (1), ibogamine (2), coronaridine (3), voacangine (4), voacangine hydroxyindolenine (5), ibogaine (6), (+)-minovincine (7), and voachalotin (8) (3) while the last one is a new compound, for which we propose the name ervayunine (9).

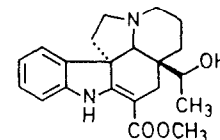


	R ¹	R ²
1	H	OH
3	H	H
4	H ₃ CO	H

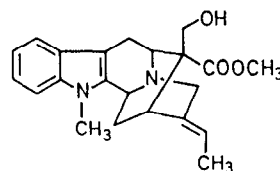
	R
2	H
6	H ₃ CO



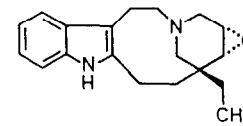
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8



9

The IR spectrum of ervayunine (9), m.p. 153–154 °C, $[\alpha]_D^{15} - 26^\circ$, C₁₉H₂₄N₂O (based on HRMS), showed absorptions at 3400, 1620, 1460, 735 cm⁻¹, while its UV spectrum possessed maxima at 229, 284, 292 nm, suggesting the presence of an indole skeleton. The mass spectrum of 9 showed characteristic fragments of voacangine at m/z 156, m/z 144, m/z 130, and m/z 140, m/z 157, m/z 249 (4), which belongs to the indole alkaloids of the quebrachamine type (5). Comparison of physical and spectral data (Table I) with those of voacangine showed that ervayunine (9) might be an enantiomer (cf. formula 11) of voacangine whose stereochemistry has been determined by X-ray

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Table I. Data comparison of compound **9** and voaphylline (**4**).

	compound 9	voaphylline (4)
molecular formula	C ₁₉ H ₂₄ N ₂ O	C ₁₉ H ₂₄ N ₂ O
mp	153–154 °C	168 °C
[α] _D	–26°	+24°
UV (log ε) nm	229 (4.50), 284 (3.83), 292 (3.81)	230 (4.52), 286 (3.85), 292 (3.84)
IR (cm ⁻¹)	3400, 3350, 1620, 1460, 735	3487, 1625, 1570
MS (m/z)	296, 267, 249, 157, 156, 144, 140, 130, 122	296, 267, 249, 157, 156, 144, 140, 130, 122

Table II. ¹H-NMR data for compound **9**.

proton	chemical shifts	proton	chemical shifts
H _(A) -3 ^b	2.72 (d)	H-14	3.19 (d)
H _(B) -3 ^b	3.35 (d)	H-15	2.97 (d)
H _(A) -5 ^c	2.28 (m)	H _A -16	4.22 (t)
H _(B) -5 ^c	2.65 (m)	H _B -16	2.78 (dd)
H _(A) -6 ^d	2.36 (m)	H _A -17	2.28 (dd)
H _(B) -6 ^d	2.88 (m)	H _B -17	1.80 (t)
H-9	7.50 (d)	H-18	0.80 (t)
H-10	7.12 (t)	H-19	1.18 (q)
H-11	7.15 (t)	H _(a) -21	1.76 (d)
H-12	7.34 (d)	H _(e) -21	2.42 (d)

$J_{3A, 3B} = 14$ Hz; $J_{9, 10} = 8$ Hz; $J_{10, 11} = 8$ Hz; $J_{11, 12} = 8$ Hz;

$J_{14, 15} = 4$ Hz; $J_{16A, 17B} = 14$ Hz; $J_{16A, 16B} = 14$ Hz;

$J_{16B, 17A} = 7$ Hz; $J_{17A, 17B} = 14$ Hz; $J_{18, 19} = 7$ Hz;

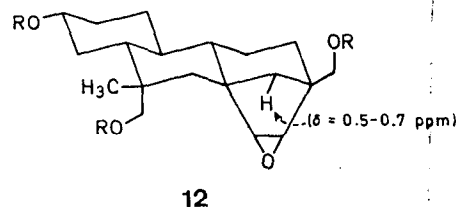
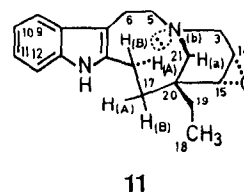
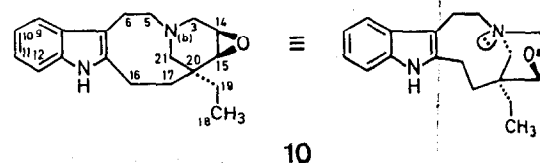
$J_{21a, 21e} = 14$ Hz.

(a) axial (e) equatorial.

^{b, c, d} Assignments may be interchanged.

Table III. ¹³C-NMR chemical shifts for compound **9** and voaphylline.

carbon compound 9	voaphylline (9)	carbon compound 9	voaphylline (9)
2	139.3	13	135.5
3	53.8	14	52.3
5	53.5	15	59.2
6	26.0	16	23.2
7	109.7	17	36.5
8	128.5	18	7.3
9	117.7	19	32.3
10	118.7	20	33.6
11	120.6	21	58.6
12	110.0		58.1



crystal diffraction (6). This suggestion is supported by spectral data of ¹H-NMR (Table II), 2D-NMR (Fig. 1), and ¹³C-NMR (Table III).

A one proton signal at $\delta = 4.22$ ppm in the 400 MHz ¹H-NMR spectrum of **9** is assigned to 16-H_(A), since it is deshielded by the unshared electron pair of N_(b) (7) as well as by the aromatic ring³. The COSY spectrum of this compound (Fig. 1) showed that the signals at $\delta = 4.22$ (t, $J = 14$ Hz) and $\delta = 2.28$ ppm (1H, dd, $J = 14$ Hz, 7 Hz) are both correlated with the signals at $\delta = 2.78$ (1H, dd, $J = 14$ Hz, 7 Hz), and $\delta = 1.80$ ppm (1H, t, $J = 14$ Hz), but no correlation between the signals at $\delta = 4.22$ and $\delta = 2.28$ ppm, nor between those at $\delta = 2.78$ and $\delta = 1.80$ ppm was observed. Thus, the chemical shift at $\delta = 2.78$ ppm should be assigned to 16-H_(B), while those at $\delta = 2.28$ and $\delta = 1.80$ ppm to 17-H_(A) and 17-H_(B), respectively.

The stereostructure of **9** showed that the three-membered epoxy ring is located in an α -position. This is in agreement with a downfield shift at $\delta = 1.76$ ppm of the axial proton at C-21. A β -position of the three-membered epoxy ring would cause a strong shielding to the C-21 axial proton (cf. formula 12) (8).

Materials and Methods

The m.p. was determined by means of a Botius melting point apparatus and was uncorrected. Optical rotation was measured on a Perkin-Elmer 241 polarimeter. ¹H-NMR, 2D-NMR, and ¹³C-NMR spectra were recorded in CDCl₃ with a Jeol FX-400 spectrometer; TMS was used as an internal standard. IR spectra were recorded with a Perkin-Elmer 683 spectrophotometer, UV spectra with a Shimadzu UV-300 spectrometer, and mass spectra with a ZAB-2F spectrometer.

The plant material was collected in February 1983 in Yunnan province (China). The botanical identification of this plant as *Ervatamia yunnanensis* Tsiang was made at the Department of Medicinal Plants (Botany) of the Institute of Materia Medica, Chinese Academy of Medical Sciences. A voucher specimen is kept at the same Department.

³ This signal was incorrectly assigned to 14-H for voaphylline by Dugan et al (4).

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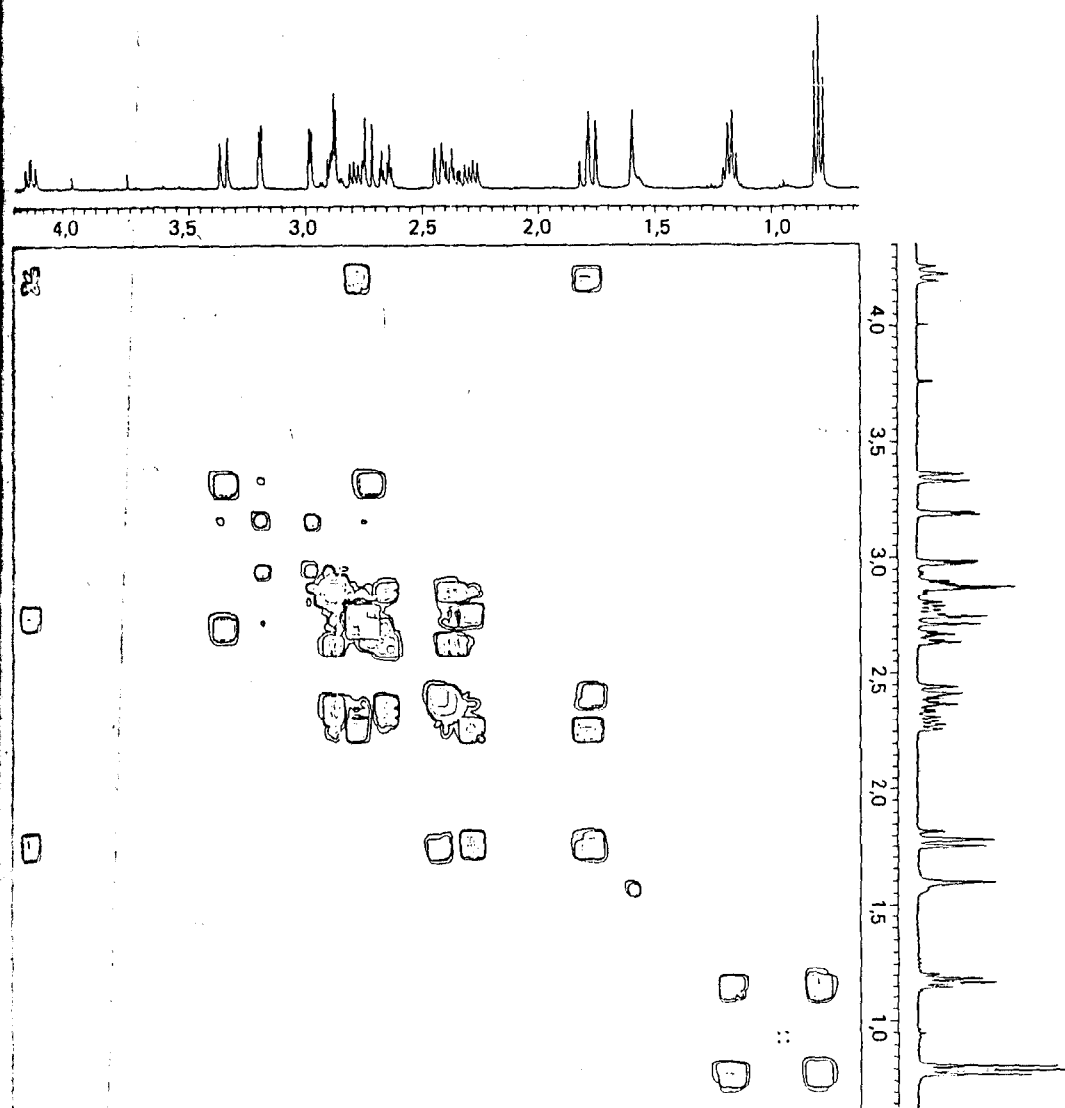


Fig. 1. Upfield region of the COSY spectrum of compound 9.

Alcoholic extraction of the air-dried root powder of *Ervatamia yunnanensis* in the classical manner gave the total alkaloids. After the "dimeric alkaloids" had been separated by filtration on the Sephadex LH-20 column, the "monomeric" fractions were further fractionated by column chromatography on silica gel and Al_2O_3 . The mixture of the "monomers" yielded heyneanine, ibogamine, coronaridine, voacangine, voacangine hydroxyindolenine, ibogaine, (+)-minovincine, voachalotin, and ervayunine.

Ervayunine (9): colourless crystals; m.p. 153–154 °C. $[\alpha]_D^{25}$: -26° ($c = 0.05$, $CHCl_3$). UV λ_{max}^{MeOH} nm (lg ϵ): 229 (4.50), 284 (3.83), 292 (3.81); IR ν_{max}^{KBr} cm^{-1} : 3400, 3350, 2910, 1620, 1460, 735; MS m/z (%): 296 (M^+ , 85), 267 (7), 249 (15), 211 (17), 210 (15), 157 (17), 156 (41), 144 (32), 143 (35), 140 (100), 130 (17), 124 (18), 122 (39), 110 (17); 1H -NMR (400 MHz, $CDCl_3$) see Table II, ^{13}C -NMR ($CDCl_3$) see Table III.

Acknowledgements

We are grateful to the Taisho Pharmaceutical Co. Ltd. for 400 MHz 1H -NMR, 2D-NMR, and ^{13}C -NMR spectra and we also thank the Department of Instrument Analysis of our Institute for UV, IR, and mass spectra.

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